dithiobisethylamine (930 mg., 6.10 mmoles), and 1-propanol (20 ml.) was refluxed for 3.5 hr. The resulting solution was cooled and poured into water (100 ml.), and the solid that precipitated was collected and dried *in vacuo;* yield 1.04 g., (83%), m.p. 180°. Recrystallization of a 150-mg. sample of the crude product from acetonitrile (45 ml.) gave 120 mg. of the disulfide as a white solid, which melted at 188° after being dried *in vacuo* over phosphorus pentoxide at 80°; λ_{max} in mμ ($\epsilon \times 10^{-3}$): 250 (20.7), 281 (17.9), 288 (18.7) at pH 1; λ_{max} at pH 7 and pH 13 unrecorded because solutions became cloudy.

Anal. Calcd. for $C_{18}H_{18}N_4S_4$: C, 51.64; H, 4.33; S, 30.64. Found: C, 51.73; H, 4.66; S, 30.72.

2-(2-Benzothiazolylamino)ethanethiol (VIII).—A 5% solution of 2,2′-[dithiobis(ethyleneimino)]bisbenzothiazole (2.09 g., 5.00 mmoles) in 2-methoxyethanol was added to a 5% solution of sodium borohydride (1.28 g., 30.0 mmoles) in methanol over a period of 5 min. The resulting solution was heated at 60° for 15 min. and then evaporated to dryness under reduced pressure. The semisolid residue was suspended in water (50 ml.) and the pH of the mixture adjusted to 8 with hydrochloric acid. The white solid was collected, washed with water, and extracted with ether (3 × 50 ml.). The ether solution, after being dried over magnesium sulfate and filtered, was evaporated to dryness under reduced pressure. The residual white solid was dried *in vacuo* over phosphorus pentoxide; yield 1.13 g. (54%); m.p. 85–86° with opaque melt (capillary); % VIII by iodometric titration 95. The ether-insoluble substance, m.p. 185°, was identified as the starting disulfide (recovery 23%).

The thiol VIII was further characterized as the *S*-2,4-dinitrophenyl derivative, which was prepared from VIII, 1-chloro-2,4-dinitrobenzene, and potassium carbonate in *N,N*-dimethylformamide. The crude 2-[2-(2,4-dinitrophenylthio)ethylamino] benzothiazole was recrystallized from an acetonitrile–water solvent pair as an orange solid, which decomposed without melting at 187–189° (capillary).

Anal. Calcd. for $C_{15}H_{12}N_4O_4S_2$: C, 47.86; H, 3.21; S, 17.04. Found: C, 47.54; H, 3.10; S, 16.68.

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Transoxazolination. Preparation of Disulfides of 2-(2-Mercaptoethylamino)-2-oxazolines

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The products obtained from the aminoethylation of several 2-thioöxazolidones underwent rearrangement in alkaline solution to 2-(2-mercaptoethylamino)-2-oxazolines, which were readily oxidized to the corresponding disulfides. The disulfides required for identification were prepared by the reaction of 2-methylthio-2-oxazolines with 2-mercaptoethylamine hydrochloride. An intermediate with anomalous properties was encountered in the latter reaction.

The rearrangement of *S*-(2-aminoethyl)isothiourea (AET), a radioprotective agent, to 2-mercaptoethylguanidine by transguanylation through a proposed cyclic intermediate in neutral or weakly alkaline solution has been described by Doherty, *et al.*[1,2] The study of this transformation was extended by these workers to a number of aminoalkylisothioureas and to 2-(2-aminoethylthio)-2-imidazoline.[3] We have recently reported the rearrangement of 2-(2-aminoethylthio)-2-thiazoline to 2-(2-mercaptoethylamino)-2-thiazolineby transthiazolination through a proposed bicyclic intermediate.[4]

In the case of the transthiazolination described, the similarity of the rings comprising the hypothetical bicyclic intermediate permitted the formation of only a single product. We have attempted to extend the rearrangement to 2-oxazoline derivatives, in which unsymmetrical bicyclic intermediates of type III would be involved.

From the reaction of 4,4-dimethyl-2-thioöxazolidone (Ia) and 2-bromoethylamine hydrobromide in refluxing isopropyl alcohol a crystalline hydrobromide of type II could not be isolated. However, when an aqueous solution of the reaction product was adjusted to pH 7.3, there was obtained, after standing, 2-(2-mercaptoethylamino)-4,4-dimethyl-2-oxazoline (IVa), isolated as the picrate, in 23% yield from the thioöxazolidone.[5] Adjustment of the solution of the reaction product to higher pH values, accompanied by aeration, resulted in the formation in 5–7% yield of the disulfide (Va) of the mercaptan.

Since sodium ethylate has been used effectively in the alkylation of 2-thioöxazolidones with alkyl halides,[6] the reaction of Ia and 2-bromoethylamine hydrobromide was carried out with this reagent. After aeration in alkaline solution, a 12% over-all yield of the disulfide dipicrate was obtained.

Similarly, the reaction of both 2-thioöxazolidone (Ib) and 4-methyl-5-phenyl-2-thioöxazolidone (Ic) with 2-bromoethylamine in the presence of sodium ethylate, followed by aeration in alkaline solution, afforded the rearranged disulfides. Bis[2-(2-oxazolin-2-ylamino)-ethyl] disulfide (Vb) and bis[2-(4-methyl-5-phenyl-2-oxazolin-2-ylamino)ethyl] disulfide (Vc), isolated as the dipicrates, were obtained in 10–15% yield.

The compounds required for identification of the rearrangement products were prepared by the reaction of the appropriate 2-methylthio-2-oxazoline with 2-mercaptoethylamine hydrochloride. The reaction of 2-methylthio-2-thiazoline with various amines[4,7] and an instance of the reaction of a 2-methylthio-2-oxazoline

(1) D. G. Doherty, R. Shapira, and W. T. Burnett, Jr., *J. Am. Chem. Soc.*, **79**, 5667 (1957).

(2) J. X. Khym, R. Shapira, and D. G. Doherty, *ibid.*, **79**, 5663 (1957).

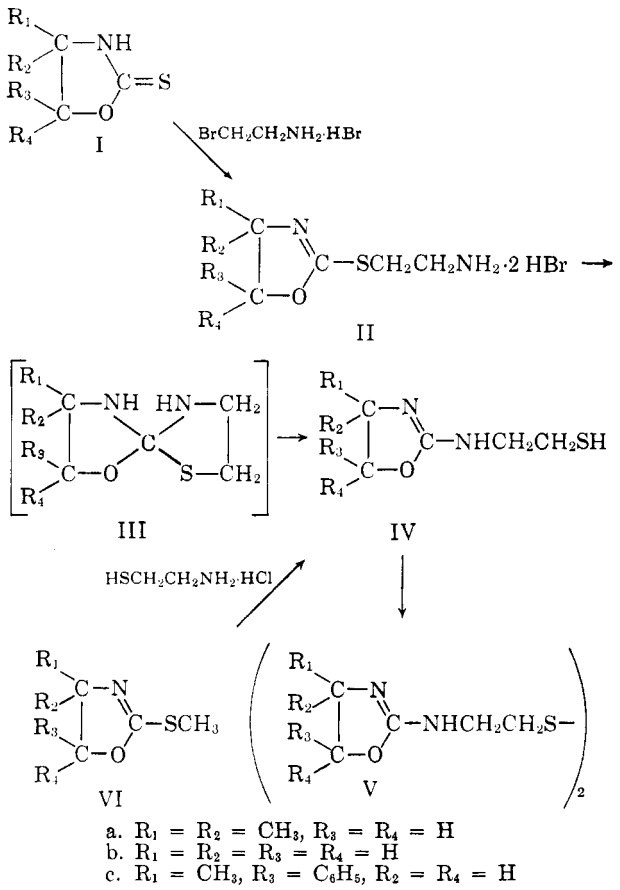
(3) J. X. Khym, D. G. Doherty, and R. Shapira, *ibid.*, **80**, 3342 (1958).

(4) R. C. Clapp, L. Long, Jr., and T. Hasselstrom, *J. Org. Chem.*, **26**, 1666 (1961).

(5) In the preparation of 2-(2-aminoethylthio)-2-thiazoline dihydrobromide from 2-thiothiazolidone and 2-bromoethylamine hydrobromide, a yield of 27% was obtained.[4] Thus the 23% over-all yield obtained here might indicate a rather high yield in the rearrangement step.

(6) L. Long, Jr., R. C. Clapp, F. H. Bissett, and T. Hasselstrom, *J. Org. Chem.*, **26**, 85 (1961).

(7) A. F. McKay, D. J. Whittingham, and M.-E. Kreling, *J. Am. Chem. Soc.*, **80**, 3339 (1958).



a. $R_1 = R_2 = CH_3$, $R_3 = R_4 = H$
b. $R_1 = R_2 = R_3 = R_4 = H$
c. $R_1 = CH_3$, $R_3 = C_6H_5$, $R_2 = R_4 = H$

with an amine[8] have been reported. The reaction of 2-methylthio-4,4-dimethyl-2-oxazoline (VIa) and 2-mercaptoethylamine hydrochloride proceeded normally to 2-(2-mercaptoethylamino)-4,4-dimethyl-2-oxazoline (IVa), which could be isolated as the picrate. Treatment of the reaction product with base in the air yielded the disulfide Va.

The preparation of the desired disulfides starting from 2-methylthio-4-methyl-5-phenyl-2-oxazoline (VIc) and 2-methylthio-2-oxazoline (VIb), however, proceeded through an intermediate with anomalous properties. When the product from VIc and 2-mercaptoethylamine hydrochloride was treated with sodium hydroxide, elementary and molecular weight analyses of the crystalline base initially obtained in 50–60% yield indicated the formula $C_{12}H_{16}N_2OS$. This formula corresponds to the mercaptan IVc rather than to the disulfide Vc. However, chemical and spectroscopic tests failed to show the presence of a mercapto group. On standing in neutral or basic solution in the air this compound was slowly converted to the disulfide Vc.

The reaction of 2-methylthio-2-oxazoline and 2-mercaptoethylamine hydrochloride yielded a crystalline hydrochloride, the properties of which indicated that it was analogous to the anomalous intermediate. In alkaline solution with aeration this compound similarly afforded the desired disulfide (Vb).

The infrared spectrum of the $C_{12}H_{16}N_2OS$ intermediate failed to show the presence of hydroxyl and primary amino groups as well as of mercapto, and its n.m.r. spectrum presented evidence that the molecule contained two NH groups. These observations have suggested the possibility that a stable compound corresponding to the proposed bicyclic intermediate in the transoxazolination (*i.e.*, IIIc) has been obtained in this case, by ring closure of the 2-mercaptoethylamino side chain. On the other hand, a strong band at 6.16 μ in the infrared spectrum would appear to indicate the presence of unsaturation in the heterocyclic ring,[6,9] which would require the formation of a side chain containing a terminal hydroxyl, amino, or mercapto group.[10] The investigation of the structure of this compound is being continued.

(8) M. Skulski, D. L. Garmaise, and A. F. McKay, *Can. J. Chem.*, **34**, 815 (1956).

Experimental[11]

2-Methylthio-4,4-dimethyl-2-oxazoline (VIa).—To a solution of 2.15 g. (0.094 g.-atom) of sodium in 100 ml. of absolute ethanol was added 12.3 g. (0.094 mole) of 4,4-dimethyl-2-thioöxazolidone (Ia).[8] A solution of 13.5 g. (0.095 mole) of methyl iodide in 50 ml. of ethanol was added, and after standing 1 hr. at room temperature the mixture was refluxed for 50 min. The alcohol was removed, and the concentrate was extracted with ether. Concentration of the ether extract and distillation afforded 9.14 g. (67% yield) of a colorless liquid, b.p. 63–64° (16 mm.).

Anal. Calcd. for $C_6H_{11}NOS$: C, 49.62; H, 7.64. Found: C, 49.47; H, 7.66.

The picrate, prepared in ethanol and crystallized from chloroform–heptane, melted at 157–159°.

Anal. Calcd. for $C_{12}H_{14}N_4O_8S$: C, 38.50; H, 3.77; S, 8.56. Found: C, 38.38; H, 3.75; S, 8.72.

2-(2-Mercaptoethylamino)-4,4-dimethyl-2-oxazoline (IVa) Picrate.—A solution of 7.88 g. (0.054 mole) of VIa and 6.4 g. (0.056 mole) of 2-mercaptoethylamine hydrochloride in 150 ml. of methanol was refluxed for 4 hr. Concentration of the solution under reduced pressure gave 12.52 g. of a viscous oil that was stored under nitrogen. Treatment of a 237-mg. portion of this oil with ethanolic picric acid solution yielded 225 mg. (55%) of picrate, m.p. 157–159°. Crystallization from ethyl acetate afforded glistening yellow plates, m.p. 159–160°.

Anal. Calcd. for $C_{13}H_{17}N_5O_8S$: C, 38.71; H, 4.25; S, 7.95. Found: C, 38.81; H, 4.16; S, 8.02.

The picrate gave a positive nitroprusside test for mercapto. Its infrared spectrum (potassium bromide) showed a mercaptan band at 3.90 μ and strong bands at 5.85 (N=C—N) and 6.10 μ.

Bis[2-(4,4-dimethyl-2-oxazolin-2-ylamino)ethyl] Disulfide (Va).—An 11.36-g. portion of the 12.52 g. of oil obtained in the previous experiment was dissolved in 170 ml. of water, and the solution was made strongly alkaline with sodium hydroxide. After aeration for several hours and cooling, filtration yielded 3.33 g. (39%) of white solid, m.p. 130–133°. Prismatic crystals, m.p. 134–136°, were obtained by crystallization from aqueous ethanol.

Anal. Calcd. for $C_{14}H_{26}N_4O_2S_2$: C, 48.53; H, 7.56; S, 18.51; mol. wt., 346. Found: C, 48.55; H, 7.36; S, 18.42; mol. wt., 345 (Rast).

Additional product could be precipitated by aeration of the filtrate. In another run, a 48% yield was obtained.

A positive nitroprusside test was obtained only after treatment with potassium cyanide, as anticipated for a disulfide.[12] The strong (N=C—N) absorption in the infrared (chloroform) was at 6.00 μ. The spectrum (potassium bromide) of the dipicrate of the disulfide had strong bands at 5.85 and 6.10 μ, similar to the picrate of the mercaptan. The dipicrate melted at 203–204.5° after crystallization from acetone.

Anal. Calcd. for $C_{26}H_{32}N_{10}O_{16}S_2$: C, 38.80; H, 4.01; S, 7.97. Found: C, 38.76; H, 4.00; S, 7.97.

IVa and Va from Rearrangement. A. Without Sodium Ethylate.—A solution of 1.32 g. (0.01 mole) of 4,4-dimethyl-2-thioöxazolidone (Ia) and 2.04 g. (0.01 mole) of 2-bromoethylamine hydrobromide in 16 ml. of isopropyl alcohol was refluxed for 4 hr. Concentration under reduced pressure afforded 4.21 g. of viscous oil. A solution of a 1-g. portion of the oil in 10 ml. of

(9) M. G. Ettlinger, *J. Am. Chem. Soc.*, **72**, 4699 (1950).

(10) The failure of the infrared spectrum to show hydroxyl, for example, might be attributable to internal hydrogen bonding to a basic nitrogen atom.

(11) Melting points were taken in capillary tubes in a Hershberg apparatus and are uncorrected.

(12) I. W. Grote, *J. Biol. Chem.*, **93**, 25 (1931).

water was adjusted to pH 7.3 by the addition of 1 *N* sodium hydroxide. After 22–23 hr. at room temperature the solution was filtered and acidified with hydrochloric acid. Saturated ethanolic picric acid solution (5 ml.) was added, and after cooling 228 mg. of crude picrate that melted from 140 to 150° was obtained. Crystallization from ethanol–acetone gave 168 mg. of yellow crystals, m.p. 155–157°. Together with 52 mg. of crystalline picrate, m.p. 153–156°, from a second crop this represented a 23% yield. Recrystallization from ethanol-acetone gave a product that was identical by mixture melting point and infrared spectrum to the picrate of IVa previously obtained.

A solution of a 1.03-g. portion of the viscous oil from the reaction in 10 ml. of water was adjusted to pH 9.5 with 1 *N* sodium hydroxide. After aeration for 4 hr. and 18–19 hr. at room temperature, filtration, acidification, and treatment with picric acid yielded a gummy precipitate. On trituration with ethanol and acetone 55 mg. (5.6%) of picrate, m.p. 193–196°, was obtained. Crystallization from ethanol–acetone afforded yellow crystals identical (mixture melting point and infrared spectrum) to the dipicrate of Va.

B. With Sodium Ethylate.—To a solution of 0.68 g. (0.030 g.-atom) of sodium in 40 ml. of absolute ethanol were added 1.96 g. (0.015 mole) of Ia and 3.06 g. (0.015 mole) of 2-bromoethylamine hydrobromide. The solution was refluxed for 2.5 hr., cooled, and filtered. The concentrate from one-half of the filtrate was dissolved in 25 ml. of water, and the pH of the solution was brought to 10.9. After about 16 hr. at room temperature with 4 hr. of aeration, the mixture was acidified and treated with picric acid. Trituration of the crude precipitate with warm ethanol and acetone yielded 373 mg. (12.4%) of picrate, m.p. 195–198°. Crystallization from acetone gave 231 mg. of disulfide dipicrate, m.p. 202.5–204°.

4-Methyl-5-phenyl-2thioöxazolidone (Ic).—The method of Ettlinger[13] for the preparation of 2-thioöxazolidones was used. A solution of 30.8 g. (0.164 mole) of α-(1-aminoethyl)benzyl alcohol (norephedrine) hydrochloride and 22 g. of 85% potassium hydroxide in 400 ml. of water and 140 ml. of dioxane was cooled in ice, and 13.1 g. (0.171 mole) of carbon disulfide in 80 ml. of dioxane was added. After 25 min. of shaking, there were added 11 g. of 85% potassium hydroxide in 200 ml. of water and 55 g. of lead nitrate in 300 ml. of water. The mixture was heated for 30 min. at 60–65°, and the black precipitate was filtered off. The precipitate that separated from the filtrate was crystallized from aqueous ethanol; 11.54 g. (36%) of glistening white plates, m.p. 92–94°, were obtained. An analytical sample melted at 93–94.5°.[14]

Anal. Calcd. for $C_{10}H_{11}NOS$: C, 62.14; H, 5.74; S, 16.59. Found: C, 62.10; H, 5.80; S, 16.84.

2-Methylthio-4-methyl-5-phenyl-2-oxazoline (VIc).—4-Methyl-5-phenyl-2-thioöxazolidone was alkylated with methyl iodide and sodium ethylate, similarly to Ia. The product was obtained (85–90% yield) as a colorless liquid, b.p. 103–105° (3 mm.). The C=N band (chloroform) was at 6.21 μ.

Anal. Calcd. for $C_{11}H_{13}NOS$: C, 63.74; H, 6.32; S, 15.47. Found: C, 63.93; H, 6.52; S, 15.43.

$C_{12}H_{16}N_2OS$ Intermediate.—A solution of 12 g. (0.058 mole) of VIc and 6.6 g. (0.058 mole) of 2-mercaptoethylamine hydrochloride in 185 ml. of methanol was refluxed for 4 hr. After cooling, it was concentrated under reduced pressure to a viscous liquid. Water (250 ml.) was added to the concentrate, and the mixture was extracted with ether to remove a little insoluble material. The aqueous solution, cooled in ice, was made basic by the addition of sodium hydroxide in portions. Crystallization of the precipitated solid (11.35 g.) from heptane–ethyl acetate gave 8.23 g. (60% yield) of white crystals, m.p. 131–134°. Recrystallization from heptane–ethyl acetate afforded 6.61 g. (48%), m.p. 134.5–136°.

Anal. Calcd. for $C_{12}H_{16}N_2OS$: C, 60.98; H, 6.83; N, 11.86; S, 13.57; mol. wt., 236. Found: C, 60.84; H, 6.91; N, 11.85; S, 13.62; mol. wt., 238 (Rast), 234 (vapor pressure osmometer).

The infrared spectrum (chloroform) showed a band at 2.91 μ (NH) and strong maxima at 6.16 and 6.69 μ. The n.m.r. spectrum[15] in deuteriochloroform contained a peak at 4.65 p.p.m., analogous to the peak at 4.73 p.p.m. attributable to NH in Va, that represented two protons and indicated two NH groups.

The pure compound did not give a positive nitroprusside test for mercapto. However, after treatment with potassium cyanide or on standing a positive test was obtained. When a solution of the compound in chloroform or ethanol was allowed to stand open to the air, a slow transformation took place, as evidenced by the formation of a strong band in the infrared spectrum at 6.01 μ, characteristic of disulfides of type V, and the simultaneous disappearance of the strong band at 6.16 μ. In ethanol this transformation was incomplete after 2 days but complete after 6 days. In aqueous ethanolic sodium hydroxide solution it was complete after three days.

The compound formed a monopicrate that separated from ethanol as fine yellow crystals, m.p. 174–176°. Its infrared spectrum (potassium bromide), similarly to that of the base, did not show a mercaptan band at 3.9 μ and showed a single strong peak at 6.10 μ.

Anal. Calcd. for $C_{18}H_{19}N_5O_8S$: C, 46.45; H, 4.11; S, 6.89. Found: C, 46.36; H, 4.19; S, 7.08.

Bis[2-(4-methyl-5-phenyl-2-oxazolin-2-ylamino)ethyl] Disulfide (Vc).—A solution of 0.5 g. of the $C_{12}H_{16}N_2OS$ intermediate in 16 ml. of ethanol and 5 ml. of 10% sodium hydroxide was allowed to stand in an unstoppered flask for 64 hr. After aeration for 2 hr., a small quantity of solid that had separated was filtered off, and the filtrate was concentrated. The concentrate was dissolved in chloroform and water, and the chloroform layer was washed with water, dried over anhydrous sodium sulfate, and concentrated to an oil. To this concentrate (0.51 g.) was added ethanolic picric acid, and treatment of the resulting crude precipitate with warm ethyl acetate yielded 0.51 g. (52%) of picrate, m.p. 197–200°. Crystallization from ethanol–acetone afforded 0.39 g. (40%) of small yellow crystals, m.p. 202–204°.

Anal. Calcd. for $C_{36}H_{36}N_{10}O_{16}S_2$: C, 46.55; H, 3.91; S, 6.90; mol. wt., 929. Found: C, 46.71; H, 3.92; S, 6.96; mol. wt., 976 (vapor pressure osmometer).

The free base of the disulfide could not be obtained as a crystalline solid. The base recovered from the crystallized picrate formed a glass that became an amorphous solid. The cyanide–nitroprusside color test given by this product and its infrared spectrum (strong N=C—N band at 6.00 μ) were consistent with its formulation as the disulfide, by comparison with the other disulfides. It was also characterized as the distyphnate, m.p. 194–197° (from ethanol–acetone).

Anal. Calcd. for $C_{36}H_{36}N_{10}O_{18}S_2$: C, 45.00; H, 3.78; S, 6.67. Found: C, 44.87; H, 3.92; S, 6.62.

The infrared spectra (potassium bromide) of both the dipicrate and distyphnate showed strong maxima at 5.85 and 6.10 μ.

Vc from Rearrangement.—The reaction was carried out with sodium ethylate, similarly to the method used for the preparation of Va by rearrangement. A solution of 0.96 g. (0.042 g.-atom) of sodium, 4.02 g. (0.021 mole) of 4-methyl-5-phenyl-2-thioöxazolidone (Ic), and 4.26 g. (0.021 mole) of 2-bromoethylamine hydrobromide in 100 ml. of absolute ethanol was refluxed for 3 hr. and filtered. After the concentrate from the filtrate had been allowed to stand in aqueous ethanolic sodium hydroxide at pH 10.7 for 4 days with intermittent aeration, there was obtained a 13.5% yield of picrate that melted from 190 to 195° and that gave an infrared spectrum nearly identical to that of the dipicrate of Vc. Crystallization from ethanol–acetone afforded a picrate, m.p. 195.5–198.5°, that represented an 11.4% yield in the reaction. Identity to Vc was established, after further purification, by mixed melting point and infrared spectra.

In another run, in which the standing in alkaline solution was omitted, the $C_{12}H_{16}N_2OS$ intermediate, isolated as the crystalline base, was obtained in 3.6% yield.

2-Methylthio-2-oxazoline (VIb).—The alkylation of 2-thioöxazolidone (Ib)[13] was carried out similarly to the alkylation of Ia. Distillation gave a 67% yield of colorless liquid, b.p. 69–71° (14 mm.).

Anal. Calcd. for C_4H_7NOS: S, 27.36. Found: S, 27.34. The picrate was identical to the one previously reported.[6]

Hydrochloride of $C_5H_{10}N_2OS$ Intermediate.—A solution of 6.6 g. (0.056 mole) of VIb and 6.4 g. (0.056 mole) of 2-mercaptoethylamine hydrochloride in 150 ml. of methanol was refluxed for 4 hr. The solution was concentrated under reduced pressure, and crystallization of the concentrate from 110 ml. of isopropyl alcohol yielded 6.58 g. of crystalline solid. Recrystallization from isopropanol gave 5.52 g. (54% yield) of colorless crystals, m.p. 115–117°. An analytical sample melted at 116–118°.

(13) M. G. Ettlinger, *J. Am. Chem. Soc.*, **72**, 4792 (1950).

(14) *threo*-4-Methyl-5-phenyl-2-thioöxazolidone, m.p. 128–130°, and the *erythro* isomer, m.p. 108–109°, prepared from the amino alcohols by a different method, have been reported by M. Kojima, *J. Pharm. Soc. Japan*, **79**, 11 (1959).

(15) Determined on a Varian A-60 spectrometer.

Anal. Calcd. for $C_5H_{11}ClN_2OS$: C, 32.87; H, 6.07; S, 17.55. Found: C, 33.04; H, 6.12; S, 17.82.

The picrate was obtained as small yellow crystals, m.p. 142–144°, from ethyl acetate.

Anal. Calcd. for $C_{11}H_{13}N_5O_8S$: C, 35.20; H, 3.49; S, 8.54. Found: C, 35.42; H, 3.60; S, 8.80.

The hydrochloride did not give a nitroprusside test for mercapto. Its infrared spectrum (potassium bromide) did not contain a mercaptan band at 3.9 μ and showed a strong band at 6.10 μ. The picrate (potassium bromide) similarly did not give a mercaptan band and exhibited a single strong band at 6.10 μ, analogously to the picrate of the $C_{12}H_{16}N_2OS$ intermediate rather than to the picrate of the mercaptan IVa.

Bis[2-(2-oxazolin-2-ylamino)ethyl] Disulfide (Vb).—To 0.6 g. of the $C_5H_{10}N_2OS$ hydrochloride in 6 ml. of water was added 3 ml. of 10% sodium hydroxide, and the solution was allowed to stand for 4 days with intermittent aeration. The white crystalline precipitate that separated amounted to 0.37 g. (78% yield), m.p. 131–133°. Crystallization from ethyl acetate afforded 0.32 g. (67%) of glistening plates, m.p. 133.5–135.5°.

Anal. Calcd. for $C_{10}H_{18}N_4O_2S_2$: C, 41.36; H, 6.25; S, 22.08; mol. wt., 290. Found: C, 41.54; H, 6.30; S, 22.02; mol. wt. (vapor pressure osmometer), 288.

The picrate separated from ethanol–acetone as fine yellow crystals, m.p. 202–204°.

Anal. Calcd. for $C_{22}H_{24}N_{10}O_{16}S_2$: C, 35.30; H, 3.23; S, 8.56. Found: C, 35.62; H, 3.38; S, 8.42.

In the infrared the base showed the strong bands at 6.0 and 6.6 μ and the picrate the strong bands at 5.85–5.9 and 6.1 μ, characteristic of the disulfides.

Vb from Rearrangement.—In the usual manner, equimolar quantities of 2-thioöxazolidone, 2-bromoethylamine, and sodium ethylate were refluxed in ethanol for 3 hr. After the product had been allowed to stand in solution at pH 9–10 for 5 days, there was obtained a 28% yield of crude picrate that melted from 170 to 182° but that gave an infrared spectrum similar to that of the dipicrate of Vb. The yield of twice-crystallized picrate, m.p. 199–201°, was 11.5%. Identity to Vb dipicrate was demonstrated after further purification, and a crystalline base identical to Vb was recovered from the picrate.

Without sodium ethylate, Vb dipicrate was obtained in very low yield.

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The Base-catalyzed Oxidation of Mercaptans. III. Role of the Solvent and Effect of Mercaptan Structure on the Rate Determining Step[1,2]

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n-Butyl mercaptan has been oxidized in dimethylformamide (DMF)–methanol and diethyleneglycol dimethyl ether (diglyme)–methanol mixtures at 23.5 ± 0.2° using sodium methoxide as the base. The relative rates of oxidation of the mercaptan decreased at the same rate in the two solvent systems as the quantity of methanol was increased in each solvent mixture suggesting that similar transition states are involved in both systems. A series of ion pair complexes which ultimately involve an intimate ion pair complex between methanol and the sodium mercaptide are suggested as possible explanations for the observed results. In addition, benzyl mercaptan, thiophenol, *p*-aminothiophenol, *p*-nitrothiophenol, and cyclohexyl mercaptan were oxidized under a variety of conditions. The observed results indicate that the rate determining step is reaction of the anion ($RS^{\ominus}$) with oxygen.

Until recently, most studies on the base-catalyzed oxidation of mercaptans (thiols) to disulfides with molecular oxygen have been limited to an aqueous sodium hydroxide media.[3] Some structural effects of mercaptans on the rate of oxidation in this medium have been observed[4] but the results have been somewhat difficult to interpret since solubilities and salting-out effects vary for the mercaptans studied. Barringer[5] has reported that N,N′-disubstituted-*p*-phenylenediamines are capable of accelerating this coupling reaction. The use of various transition metal phthalocyanines and other organic chelates in basic media has also been recommended.[6] In the latter case, the rate-limiting step appears to be diffusion of oxygen and the mercaptide ion to the surface of the catalyst.[7] We have recently observed in these laboratories[1] that various dipolar and ethereal solvents greatly enhanced the homogeneous, base-catalyzed oxidation rate of *n*-butyl mercaptan with molecular oxygen.

The present study was undertaken to determine how the addition of a hydroxylic material (methanol) to an aprotic base–solvent system would effect the rate of oxidation of *n*-butyl mercaptan. Further, it also seemed of interest to ascertain how the rate of oxidation varied with the structure of the mercaptan since this would provide information on the rate determining step in this reaction.

Results

One-tenth of a mole of *n*-butyl mercaptan was oxidized in DMF–methanol and diglyme–methanol mixtures at 23.5 ± 0.2° under a constant oxygen pressure of one atmosphere. 0.2 mole of sodium methoxide was used in each oxidation reaction. Each reaction was carried out to about 30% completion. The amount of mercaptan converted to the disulfide was determined from the amount of oxygen consumed as a function of time according to the derived first-order rate expression. The apparent first-order rate constants obtained for the oxidation of *n*-butyl mercaptan to the disulfide in each hydroxylic–aprotic solvent mixture are summarized in Table I and calculated relative to the rate obtained in

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